

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 4

Specifically, claim 18 is amended to recite that the antagonist is administered "to specifically inhibit the activity if the integral membrane protein." Support for this amendment is also found throughout the Specification, including at least page 6, lines 8-14.

Claims 18 and 36 are amended to recite an antagonist "consisting essentially of" rather than "comprising" at least four consecutive amino acid residues from a transmembrane domain. Applicants acknowledge that the "comprising" language may have encompassed the *entire* transporter or receptor protein, and this was not intended. In contrast, the invention is clearly directed to peptides which consist essentially of a single transmembrane domain or a portion of a single transmembrane of a transporter or receptor. Thus, for example, the Specification teaches:

"The antagonist peptide for a particular membrane protein may have the entire amino acid sequence of a transmembrane domain or may comprise a portion or fragment of the transmembrane amino acid sequence."

Fragments of a transmembrane amino acid sequence may be selected by truncation of one or more amino acids from the amino terminus of the transmembrane amino acid sequence, by truncation of one or more amino acids from the carboxy terminus or by truncation of one or more amino acids from both amino and carboxy termini." (page 7, line 29 - page 8, line 3)

"The present invention provides antagonist peptides which correspond to the amino acid sequence of an integral membrane protein transmembrane domain, fragments of such a sequence and peptides which include the amino acid sequence of an integral membrane protein transmembrane domain or fragments thereof.

The present invention provides antagonist peptides comprising amino acid sequences corresponding to at least four, preferably ten and more preferably from fifteen to twenty consecutive amino acids of an integral membrane protein transmembrane domain." (page 8, lines 14-24)

Therefore, Applicants submit that there is ample support in the Specification for the amendment.

Claims 32 and 35 are each amended to recite use of the methods in the treatment of only one of two previously recited conditions. Therefore, because these amendments strictly narrow these claims, there is support for the amendments in the claims 32 and 35 as originally filed.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 5

Claims 62-64 are amended to depend from claim 22 rather than claim 60 and to further limit the "integral membrane protein" of claim 22 rather than the "tyrosine kinase receptor" of claim 60. This amendment merely corrects a drafting error and, because the amended claims strictly narrow claim 22, there is support for the amended claims in claim 22 as originally filed.

With respect to amendments to the Specification, an amendment is made to page 42 which corrects a reference to "Fig. 5f" to a reference to "Fig. 5g". Applicants submit that it would have been apparent to one of ordinary skill in the art, from the text preceding the reference and from the figure labels, that Fig. 5g was intended. Similarly, pages 42 and 43 of the Specification have been amended merely to move the position of two paragraphs describing Fig. 6 and relating to the experiment entitled "Inhibition of  $\alpha$ 1A-adrenergic Receptor Activity", described at the bottom of page 42 to page 43. These paragraphs were inadvertently misplaced during the preparation of the application and, Applicants submit, it would have been apparent to one of ordinary skill in the art that these paragraphs properly belong in the description of the experiment on  $\alpha$ 1A-adrenergic receptor activity, as they refer to further administration of phenylephrine and to the results shown in Fig. 6.

Rejection of Claims 18, 20-37 and 60-65 under 35 U.S.C. §112, first paragraph

Claims 18, 30-37, and 60-65 were rejected under 35 U.S.C. §112, first paragraph, as "containing subject matter which was not described in the Specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention."

Specifically, the Office Action notes that Applicants, in their previous response, had raised six points to traverse a previous and similar rejection, and the Office Action then challenges each of these points. Therefore, Applicants wish to clarify their previous submissions, point by point, in response to the issues raised:

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 6

1. The Office Action objects that peptides "associated with specific receptor overactivity" have not been claimed, that the claims encompass any G-protein receptor dysfunction, including disease states in which "lack of activity" characterizes the disease state, that abnormal function of D2 receptors is not equivalent to "overactivity," and that the claims do not recite using any *specific* peptide to *specifically* inhibit D2 receptors.

First, Applicant note that the claims, as amended, refer to the treatment of "a disorder for which administration of an *antagonist* of an integral membrane protein . . . is indicated" by administration of a described peptide "to *specifically inhibit* the activity of the integral membrane protein." By definition, an antagonist inhibits the activity of a receptor or transporter and, therefore, Applicants submit that an antagonist would not be indicated to specifically inhibit integral membrane protein activity in a disorder characterized by "lack of activity" of the protein.

More particularly, the Specification teaches that peptides selected in accordance with the invention may be used to treat disorders associated with specific receptor overactivity such as schizophrenia, which is associated with overactivity of the D2 dopamine receptor, as described at page 10, lines 19 to 22 of the Specification.<sup>1</sup> The Specification also teaches that antipsychotic drugs which block the D2 dopamine receptor have been used beneficially in neuropsychiatric diseases, and notes that antagonists of the D2 dopamine receptor are useful for treatment of schizophrenia, Huntington's disease and Tourette's syndrome.

With respect to Parkinson's disease, it is irrelevant to the present invention that Parkinson's disease is characterized by dopamine receptor *inactivity*, because one of ordinary skill in the art would recognize that a dopamine receptor *antagonist* is not indicated in Parkinson's disease. Applicants have neither suggested nor claimed the treatment of Parkinson's disease with the antagonist peptides of the invention.

Finally, contrary to the statement in the Office Action, the claims which refer to treatment of schizophrenia, Huntington's disease and Tourette's syndrome do refer to *specific* peptides

---

<sup>1</sup> Applicants note that the wrong page reference was provided in the previous Response. This explains why, as the Office Action correctly states, "page 12, lines 19-22, mentions nothing about schizophrenia." The correct citation is to page 10, lines 19-22. Applicants apologize for the error.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 7

derived from the transmembrane domain of the D2 dopamine receptor (e.g., claim 27) and, as amended, do recite that the peptides are administered "to specifically inhibit" that receptor.

2. The Office Action objects that there is "contradictory guidance" on the use of antagonists of the  $\beta$ 1-adrenergic receptor, that there is insufficient guidance for the use of antagonists of the  $\alpha$ 1A-adrenergic receptor, and that practice of the invention would require undue experimentation.

With respect to  $\beta$ 1-adrenergic receptors, the Specification clearly teaches that inhibition of  $\beta$ 1-adrenergic receptor activity by means of a peptide derived from the  $\beta$ 1-adrenergic receptor TMVII peptide led to a reduction of the heart rate of a live rat, as described in the example beginning at p. 41, line 17, as amended herein (i.e., excluding the paragraphs moved to p. 43). Therefore, the Specification provides a teaching and reasonable expectation that peptides derived from the  $\beta$ 1-adrenergic receptor TM domains are antagonists that are useful for the control of cardiac arrhythmia.

With respect to  $\alpha$ 1A-adrenergic receptors, the Specification clearly teaches that use of a peptide derived from the TMVII domain of the  $\alpha$ 1A-adrenergic receptor had an antagonistic effect on  $\alpha$ 1A-adrenergic receptor activity, resulting in a lowering of blood pressure in a live rat, as described in the example beginning at p. 42, line 32, as amended herein (i.e., including the paragraphs moved from p. 42). Therefore, the Specification provides a teaching and reasonable expectation that peptides derived from the  $\alpha$ 1A-adrenergic receptor TM domains are antagonists that are useful as hypotensive agents.

Therefore, the  $\alpha$ 1A- and  $\beta$ 1-adrenergic receptor antagonist peptides, which are *specific* peptides which *specifically inhibit* those receptors, and which are clearly described in the Specification and specifically recited in claims 12-15, offer new agents for treating hypertension and cardiac arrhythmia, respectively. Applicants respectfully submit that it does not entail undue experimentation to test peptides, as shown in the examples in the Specification, based upon the sequences disclosed in the Specification, to determine their suitability as adrenergic receptor antagonists.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 8

3. The Office Action objects that the claims do not recite *specific* peptides to *specifically* inhibit *specific* adenosine receptors, that there is insufficient guidance on the use of the methods (particularly for the disorders of claim 28 "that have no known cause"), and that there can be no expectation that administering transmembrane-specific peptides for affecting one symptom of one disorder can be extrapolated to treating the full scope of symptoms of the disorder.

Respectfully, Applicants note again that the claims relate to a method of treating "a disorder for which administration of an *antagonist* of an integral membrane protein . . . is *indicated*." The Specification does not attempt to list all diseases for which such antagonists are indicated, nor to list which integral membrane proteins are associated with each and every disease. Such a teaching is not required because it goes beyond the scope of the claimed invention. Some diseases associated with overactivity of integral membrane proteins have already been identified, and it is very likely that more will be identified in the future. However, it is Applicants' invention, and the teaching of the Specification, that disorders for which treatment with an *antagonist* of an integral membrane protein *is indicated* can be treated by administering an antagonist peptide derived from the amino acid sequence of a transmembrane domain of the protein to specifically inhibit the activity of the integral membrane protein. The Specification describes a number of these diseases and their associated receptors, and provides working examples of the utility of the invention, in a manner which is sufficient to illustrate the invention and to enable one of ordinary skill in the art to practice it without undue experimentation. In addition, Applicants do, in fact, teach *specific* peptides which may be used to *specifically inhibit* the *specific* receptors from which they are derived. Applicants respectfully submit that no more is legally required.

With respect to the disorders of claim 28, Applicants note that although schizophrenia, Huntington's disease and Tourette's syndrome are undoubtedly complex diseases, "existing antipsychotic drugs have been shown to selectively block the D2 dopamine receptor", as taught at page 20, lines 13-14, of the Specification. Thus, these existing drugs, which are antagonists of D2 receptor, are regarded as useful by those of skill in the art. The Office Action cites no

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 9

evidence in support of the argument that the new D2 dopamine receptor antagonists disclosed in the present application will not have a similar expectation of usefulness in these conditions.

4. The Office Action objects that EGF receptors are not representative of all neoplastic growth in cancer because all neoplasms are not caused by dysfunction of the EGF receptor. Applicants agree. However, the claims encompass only treatment of such disorders in which administration of an *antagonist* of an integral membrane protein *is indicated*. An example of EGF receptor-associated neoplastic growth was provided in the Specification to illustrate how one of ordinary skill in the art can recognize a disorder in which an antagonist of an integral membrane protein is indicated, without undue experimentation. The claims are not directed to treating all neoplastic growths or, indeed, any other conditions in which administration of an antagonist of an integral membrane protein is not indicated.

5. The examples relating to GABA receptors and monoamine transporters were provided for the same reasons as the examples relating to the EGF receptors discussed above.

6. The Office Action objected that claims 18, 22g, 25h, 26h, 30h, 33h and 36 continue to recite the phrase "effective fragment or analogue thereof." These claims are each amended herein to delete that phrase and, therefore, Applicants respectfully submit that the amendment overcomes the grounds for rejection and request that the rejection be withdrawn.

**Rejection of Claims 62 and 64-65 under 35 U.S.C. §112, second paragraph:**

Claims 62 and 64-65 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claims 62-64 included a drafting error which confused the dependency and the antecedent basis of the claims. These claims have been amended to correct the errors which led to this rejection. Applicants respectfully submit that the amendment overcomes the grounds for rejection and request that the rejection be withdrawn.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 10

**Rejection of Claims 18, 20-22, 36 and 60-61 under 35 U.S.C. §102(b)**

Claims 18, 20-22, 36 and 60-61 were rejected as being anticipated by Lofts et al. Again, Applicants must respectfully disagree with the characterization of the teachings of Lofts et al. in the Office Action.

Contrary to the statement in the Office Action, Lofts et al. does not teach "treatment of nude mice with an effective amount of a WT peptide sequence comprising at least one transmembrane domain of the neu/EGF integral membrane protein". Nor does Lofts teach administration of isolated transmembrane peptides to nude mice in which treatment with an antagonist of an integral membrane protein is indicated.

Rather, Lofts studied the effect of causing neu-transformed cancerous cells to express within themselves portions of the neu oncogene. The experiment was conducted both *in vitro* and *in vivo*. The growth of these transformed cells was studied in nude mice, as such mice do not reject foreign tissue, thus allowing the effect of neu oncogene expression within the tumor cells on tumor cell growth to be observed. This model system is not in any way analogous to the claimed invention.

As noted previously, the authors of this reference did not conceive of the use of isolated integral membrane protein transmembrane domain peptides as potential pharmaceuticals, since they indicate their belief that it is important that the sequences in question must be produced by expression within the cell and must be inserted by the cell into the cell membrane. This would not suggest to one skilled in the art that isolated peptides could be administered as drugs.

For anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present. MPEP 706.02. A rejection based on 35 U.S.C. 102(b) can be overcome by persuasively arguing that the claims are patentably distinguishable from the prior art, or by amending the claims to patentably distinguish over the prior art. MPEP 706.02(b).

The presently claimed invention includes a method of treating a disorder for which administration of an antagonist of an integral membrane protein having at least one transmembrane domain is indicated, comprising administering to the mammal an effective amount

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 11

of an antagonist peptide consisting essentially of at least four consecutive amino acid residues from the amino acid sequence of a transmembrane domain of the protein to specifically inhibit the activity of the integral membrane protein. Lofts et al. does not teach this method. Specifically, Lofts et al. does not teach a method of treatment of a disorder for which administration of an antagonist of an integral membrane protein is indicated, and Lofts et al. does not teach administering isolated peptides. Therefore, Lofts et al. cannot anticipate the claims and Applicants request that the rejections based upon Lofts et al. be withdrawn.

Rejection of Claims 18, 20-24, 29, 36, 37, 60 and 61 under 35 U.S.C. §102(e)

Claims 18, 20-24, 29, 36, 37, 60 and 61 were rejected as anticipated by Murphy et al.

The Office Action states that Murphy et al. teach the use of dopaminergic and adrenergic G-protein-coupled transmembrane receptor peptides in pharmaceutical compositions to "treat or prevent" G protein-related diseases.

However, the Office Action relies on only select portions of the Murphy et al. disclosure to support this rejection, while ignoring other portions of the disclosure which teach in opposite directions and do not support the rejection.

The teachings of Murphy et al. must be considered as a whole, and as one skilled in the art would understand it, having read and absorbed the whole of the teachings. See, for example, In re Wesslau, 147 USPQ 391, 393 (CCPA 1965), where it was held that it is impermissible to pick and choose from a reference "only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art" (emphasis added).

It is respectfully submitted that, having reviewed all of the teachings of Murphy et al., one skilled in the art would not have appreciated the specificity of inhibition of the activity of an integral membrane protein achieved by administration of an antagonist peptide consisting essentially of at least four consecutive amino acid residues selected from the amino acid sequence of a transmembrane domain of that integral membrane protein, as disclosed and claimed in the present application.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 12

Specifically, Murphy et al. proposes that peptides corresponding to portions of the amino acid sequence of G-protein-coupled receptors, or peptides somewhat resembling such portions, will mimic the receptors and bind to ligands of the receptors (see, for example, column 6, lines 43-46). Murphy et al. proposes that these peptides will "*modulate* the binding of GPR ligands to GPRs, such as *inhibition or enhancement* of binding" (column 8, lines 35-38, emphasis added). Murphy et al. offers no guidance as to how to select peptides for either inhibition or enhancement of binding, and certainly does not teach that peptides derived from a transmembrane domain of an integral membrane protein will act as antagonists of that protein.

Further, although Murphy et al. proposes as an object of the invention that GPR peptides can be used as potential modulators of G protein-coupled receptor function, Murphy et al. shows absolutely no evidence of any effect of the described peptides on the function of any G protein-coupled receptor. In fact, Murphy et al. shows no data at all involving any G protein-coupled receptor. Therefore, Murphy et al. do not disclose specific inhibition of any G protein coupled receptor activity, and certainly does not teach that peptides derived from a transmembrane domain of an integral membrane protein will act as antagonists of that protein.

The single example in Murphy et al. (columns 37-39) describes the binding of a peptide derived from the dopamine D2 receptor to radioactively labeled spiperone, a ligand of the dopamine D2 receptor. The preparation did not contain any D2 receptors, and neither receptor binding nor receptor function was examined. There is, therefore, no demonstration of any effect of the tested peptide on receptor function, and it cannot be concluded from this experiment that the tested peptide would have affected ligand binding or receptor function in any way. Therefore, Murphy et al. do not disclose specific inhibition of D2 dopamine receptor activity, and certainly does not teach that peptides derived from a transmembrane domain of an integral membrane protein will act as antagonists of that protein.

---

In contrast, the present inventors have shown that antagonism of an integral membrane protein receptor is highly specific to the transmembrane peptide of that receptor. At pages 37-38 of the present Specification, an experiment is described in which it was shown that the human dopamine D2 receptor is disrupted by a D2-TM VII peptide (page 37, lines 10-15), whereas the

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 13

dopamine D1 receptor was unaffected by this D2-TM VII peptide (page 38, lines 2-5). The dopamine D2 receptor was also unaffected by a transmembrane peptide from the  $\alpha$ -adrenergic receptor.

Furthermore, the present inventors have shown that a dopamine D2 receptor transmembrane peptide acted *in vivo* in rats as a dopamine D2 receptor antagonist (see, particularly, page 40, lines 13-15), whereas a transmembrane domain peptide derived from the  $\beta$ -adrenergic receptor had no antagonist activity (see Figure 3, panels A and C).

It is clear from reading Murphy et al. as a whole, and considering the range of peptides which are proposed for use, that Murphy et al. failed to conceive of the specificity of receptor antagonism achieved by use of a transmembrane domain peptide of the receptor itself, but not of related receptors, as disclosed in the present application. Indeed, it is unclear from Murphy et al. whether such peptides would be expected to cause inhibition or enhancement of receptor activity.

In addition, not only does Murphy et al. suggest using peptides which comprise an algorithmically-devised consensus sequence reflecting the various transmembrane domains of one particular receptor, Murphy et al. goes further to describe consensus sequences reflecting the transmembrane domains of different receptors within a group of related receptors (e.g. Figure 5 shows a consensus peptide reflecting a mixture of the transmembrane sequences of the dopamine D1 and D2 receptors).

Murphy et al. even suggests, at column 17, preparing consensus polypeptides across several, perhaps as many as 500, G-protein receptors. If one cannot produce the specific antagonism of a D2 dopamine receptor noted by the present inventors by use of the transmembrane domain of a dopamine D1 receptor, one certainly would not expect to be able to produce the specific antagonism of a receptor by using a blended amino acid sequence across 500 different and totally unrelated G-protein receptors.

---

Furthermore, Murphy et al. actually suggests, at column 9, line 66, to column 10, line 5, that "a 'GPR polypeptide' of the present invention includes polypeptides having a 'GPR amino acid sequence' which substantially corresponds to at least one 10 to 50 amino acid fragment and/or

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 14

consensus sequence of a known GPR or a group of GPRs." It is later suggested only that the GPR polypeptide preferably "substantially corresponds to a transmembrane domain of a GPR or group of GPRs as a consensus sequence" (column 10, lines 10-13).

The present inventors have shown quite clearly that the specific antagonistic effect on receptor function of the present invention is obtained using transmembrane domain peptides and cannot be achieved by using peptides from other portions of the receptor molecule. For example, in the experiment described at pages 37-38 of the present application, it was shown that the human dopamine D2 receptor was disrupted by a D2-TM VII peptide but was unaffected by two peptides from cytoplasmic domains of the D2 receptor.

Therefore, taking the teachings of the Murphy et al. reference as a whole, one skilled in the art learns that any segment of any GPR protein, or any consensus sequence representing a blending of anything up to 500 different G-protein receptors, can be used to interfere with ligand binding to a receptor. Yet there is no demonstration in Murphy et al. of interference with ligand binding to a receptor by any described peptide, far less any demonstration of what effect such interference might have on receptor function

There is nothing in the teachings of Murphy et al. of peptides selected from any portion of a GPR receptor, or of consensus peptides blending the characteristics of up to 500 unrelated G-protein receptors, to bind ligands (with no described effect on receptor activity) to suggest the specific antagonism of a receptor's activity by transmembrane peptides from that receptor, or fragments or substituted variants thereof, as described and claimed in the present invention. In fact, Murphy et al.'s description of peptides selected from any portion of a GPR receptor, and of consensus peptides mixing the sequences of large numbers of unrelated receptors, teach away from the requirements for specific antagonism of receptor activity, as described by the present inventors.

---

For anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present. MPEP 706.02. A rejection based on 35 U.S.C. 102(b) can be overcome by persuasively

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 15

arguing that the claims are patentably distinguishable from the prior art, or by amending the claims to patentably distinguish over the prior art. MPEP 706.02(b).

The presently claimed invention includes a method of treating a disorder for which administration of an antagonist of an integral membrane protein having at least one transmembrane domain is indicated, comprising administering to the mammal an effective amount of an antagonist peptide consisting essentially of at least four consecutive amino acid residues from the amino acid sequence of a transmembrane domain of the protein to specifically inhibit the activity of the integral membrane protein. Murphy et al. does not teach this method. Specifically, Murphy et al. does not teach that peptides derived from a transmembrane domain of an integral membrane protein will act as antagonists of that protein and may be used to specifically inhibit the activity of the protein from which they are derived.

Applicants: Ng et al.  
U.S.S.N.: 08/670,119  
Filed: June 25, 1996  
Page 16

### SUMMARY

Claims 18, 20-37, and 60-65 are pending in the application. Claims 18, 32, 35, 36, and 62-64 are amended herein. The Specification is amended to correct typographical and formatting errors. Applicants submit that no new matter is added by any of the amendments.

Applicants request that the Examiner reconsider the application in light of the foregoing Preliminary Amendment and Remarks, and respectfully submit that the claims, as amended, are in condition for allowance. If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues, and to work with the Examiner toward placing the application in condition for allowance.

Applicants believe that no additional fees are necessitated by the present Preliminary Amendment. However, in the event that any additional fees are due, the Commissioner is hereby authorized to charge any such fees to Attorney's Deposit Account No. 20-0531.

Respectfully submitted,

Date: Jan. 25, 1999  
Reg. No. 38,349  
Tel. No. (617) 248-7362  
Fax No. (617) 248-7100

Michael J. Twomey  
Michael J. Twomey  
Attorney for Applicants  
Testa, Hurwitz, & Thibeault, LLP  
High Street Tower  
125 High Street  
Boston, MA 02110

395MJT7434/2.A717630-1

---

**TESTA, HURWITZ & THIBEAULT, LLP**

---

ATTORNEYS AT LAWHIGH STREET TOWER  
125 HIGH STREET

OFFICE (617) 248-7000

BOSTON, MASSACHUSETTS 02110

FAX (617) 248-7100

**TELECOPY COVER SHEET**

---

*Equipment Operator Contact Number: 617-248-7362. Please call if you do not receive all the pages.*Date: January 25, 1999TO: Name: **Examiner R. Hayes**  
Art Unit: **1645**

Telephone:

Fax: **(703) 308-4242**FROM: Sender: Michael J. Twomey, Reg. No. 38,349Number of Pages **INCLUDING** This Cover Sheet: 17Client: **7434/2 (SIM-001)**

Comments:

---

This facsimile is subject to attorney-client privilege and contains confidential information intended only for the person(s) named above. If you have received this facsimile in error, please notify us immediately by telephone and destroy the original transmission without making a copy.

---

Sent by:

395MJT9901/144525\_1

Date Sent: January 25, 1999

Time Sent \_\_\_\_\_